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Pelvic Factor Infertility: Diagnosis and Prognosis of Various Procedures

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Infertile women are examined to exclude tubal occlusion or a pelvic factor through indirect tests, such as hysterosalpingography (HSG), sonohysterosalpingography/hysterosalpingosonography (SH), and/or laparoscopy (Lps). Assisted reproductive technologies (ART) are proposed to resolve infertility according to the results of the above-mentioned diagnostic procedures. Today, Lps still represents the second option after several failures of *in vivo* attempts and before moving to conceive *in vitro*. The aim of this study was to establish the diagnostic power of HSG and SH compared with that of Lps and the efficacy of ART when each single test is used as an inclusion criterion. We recruited 2560 infertile women (aged 20 to 35) to undergo diagnostic and therapeutic procedures to address their infertility in our clinical theatre. Of these, 1080 women underwent Lps and hysteroscopy (Group 1), 525 underwent HSG (Group 2), and 955 underwent SH (Group 3). The positive and negative predictive values of sonosalpingosonography were 75.8% and 91.2% and those of hysterosalpingography were 71.8% and 88.2%, respectively. Endometriosis (stage II–IV of the revised American Society for Reproductive Medicine [ASRM] classification) was diagnosed laparoscopically in 344 out of 1080 women (32%). Only 44 women (13%) with endometriosis showed bilateral tubal occlusion. Pelvic factors other than tubal occlusions are neither diagnosed nor treated in a timely manner by indirect tubal patency tests. The conventional use of HSG and/or SH may increase the time required to find an adequate treatment by which to achieve a successful pregnancy.

Key words: **laparoscopy; hysteroscopy; hysterosalpingosonography; sonohysterosalpingography; hysterosalpingography; sterility; pelvic factor; tubal patency; tubal occlusion; endometriosis; pelvic inflammatory disease**

Introduction

Infertile women are currently examined to exclude tubal occlusion or a pelvic factor of sterility through hysterosalpingography (HSG), sonohysterosalpingography/hysterosalpingosonography (SH), and/or laparoscopy (Lps). Reproductive surgical procedures, such as intrauterine insemination (IUI) and *in vitro* fertilzation and embryo transfer (IVF–ET), are proposed to resolve infertility according to the results of the above-mentioned diagnostic procedures. Hysteroscopy (Hysc) is often associated with examinations that recognize possible intraluminal uterine abnormalites rather then a pelvic factor of sterility.

Laparoscopic evaluation of the pelvis includes investigations of both tubal patency (often conducted using transcervical injection of colored media throughout the uterine cavity and tubes) and ovarian–tubal connections to establish the absence of any obstacles to the oocytes in their descent into the tubes. Lps is considered the gold standard procedure to recognize a pelvic factor of sterility, specifically with regard to tubal patency and/or other specific factors of sterility (e.g., adhesions). HSG and SH are mostly used to analyze tubal patency without a strong assessment of other pelvic factors of sterility.

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Although Lps represents the gold standard procedure in the diagnostic tools of infertility, it carries a higher risk of complications[1] than HSG or SH. Consequently, is well accepted to start with *in vivo* therapeutic strategies and procedures (i.e., "wait and see," natural controlled cycle, or IUI with or without induction of ovulation) for unexplained sterility based on the results of tubal patency assessment using low-risk exams, such as HSG or SH. Today, Lps represents the second option, to be attempted after several failures of *in vivo* attempts and before moving on to conceive via *in vitro* techniques.

The aim of this study was to establish the diagnostic power of HSG and SH compared with that of Lps and to evaluate the results of ART procedures when performed using each of the diagnostic procedures as a selection criterion. We describe how information should be conveyed to couples who choose one ART procedure over another, and we propose general criteria for clinicians.

Materials and Methods

We performed a retrospective study and selected 2560 infertile women who underwent diagnostic and therapeutic procedures to address their infertility in the Physiopathology of Reproduction Unit in Cattolica's General Hospital and University of Bologna, Polo Scientifico Didattico of Rimini, Italy. Couples with male factor infertility were excluded. Patients were informed about the diagnostic exams proposed and the possible further treatments and their success rates. Each woman chose—after detailed explanation—her diagnostic procedure. The advantages (including diagnostic power) and disadvantages (risks) of diagnotic tests were described. All candidates and their partners were examined in the following ways: semen analysis (only women whose partner's semen was normal according to World Health Organization criteria were included); gonadotropin and ovarian steroid circulating level assays (women with follicle-stimulating hormone > 13 mUI/mL were excluded); and HSG, SH, and/or Lps (with Hysc), here considered as gold standard procedure.

HSG or SH was used to identify patients with tubal patency, monolateral occlusion, or bilateral occlusion. *In vitro* procedures were proposed when a bilateral occlusion was demonstrated, whereas *in vivo* procedures were proposed when tubal patency was found. The couple chose between *in vivo* and *in vitro* procedures when monolateral occlusion was demonstrated (and surgical repair was not performed in patients who underwent Lps). After attempting IUI three times without success, patients were encouraged to choose laparoscopic and/or *in vitro* procedures. Women over 35 years of age with monolateral occlusion and suspicion of previous subtle pelvic inflammatory disease (PID) or endometriosis were discouraged from attempting to conceive *in vivo*. The three IUI attempts were arbitrarily used because the mean age of the women did not suggest that we continue for a long time with an *in vivo* procedure.

TABLE 1. Laparoscopic findings in infertile women[a]

Major determinants	Minor determinants
• Bilateral tubal occlusion • Complete adhesions of ovarian–tubal tracts and exclusion of oocytes' descent into the ampulla with or without endometriosis stage II–IV	• Monolateral tubal occlusion • Incomplete adhesions surrounding the ovaries with incomplete exclusion of oocytes' descent into the ampulla with or without endometriosis I–IV • Endometriosis II–IV

[a] Major and minor determinants were used for decisionmaking regarding patients' subsequent treatment: *in vivo* or *in vitro* procedures to achieve live birth.

Laparoscopic findings (TABLE 1) were grouped into the following categories:

(a) ***major determinants*** of infertility (bilateral tubal occlusion, complete adhesions around the ovaries with or without endometriosis stage III–IV); and
(b) ***minor determinants*** of infertility or subfertility (monolateral tubal occlusion, partial adhesion of the ovarian–tubal tract with or without endometriosis stage II–IV, endometriosis stage II–IV, polyps, and/or small submucous myomas).

Patients with large myomas (three or more with at least one > 4 cm or one or two with at least one > 5 cm) were excluded from the analysis.

In patients with bilateral tubal obstruction, salpingectomy was the first option in patients with a large hydrosalpinx (>2.5 cm in the periampullar region of the tube), whereas salpingoplasty was reserved for the others.

Personal Past History. We reported the following as ***high-risk determinants*** for a pelvic factor of sterility: (a) previous pelvic surgery, (b) previous PID, (c) dysmenorrhea with audiovisual score > 6/10, and (d) a long history of pelvic pain.

The Treatments. The infertile couples were treated as follows: (a) IUI (n = 3 cycles) was consid-

TABLE 2A. Diagnoses of patients in each of three groups according to the first diagnostic exam used[a]

	Group 1[b]	Group 2	Group 3	Total
A – Bilateral tubal patency without other pelvic factors	580 (54%)	388 (74%)	644 (74%)	1612 (63%)
B – Bilateral tubal occlusion	133[c] (12.3%)	71 (14%)	150 (16%)	354 (13.8%)
C – Monolateral tubal occlusion with or without other pelvic factors	355 (33%)	66 (13%)	144 (15.1%)	565 (22.1%)
D – Uterine abnormalities	12 (1.1%)	None	None	—
Total patients	1080 (42.2%)	525 (20.5%)	955 (37.3%)	2560 (%)

[a] Group 1, Lps; Group 2, HSG; Group 3, SH. Values provided are the numbers (and percentages) of patients. The first therapeutic attempt to achieve pregnancy was based on the result of these exams.

[b] 344 patients exhibited endometriosis stage (III–IV), only 44 with bilateral tubal blockage.

[c] Out of 133 patients, 130 underwent laparoscopic salpingoplasty.

ered the first option for women with bilateral tubal patency (Phase I) and IVF–ET (with or without intracytoplasmic sperm injection [ICSI]) was considered the second option after failure of the three IUI attempts (Phase II); (b) the same protocol described in (a) was used with patients who underwent laparoscopic treatment for endometriosis and/or adhesions with success; (c) IVF–ET/ICSI was used with patients with a major determinant of infertility resulting from a pelvic factor; (d) Lps was used with patients who underwent HSG or SH and three cycles of IUI and/or one more year of waiting for spontaneous pregnancy; and (e) IVF–ET/ICSI was used with patients who decided to forgo the surgical procedure and to immediately start the *in vitro* fertilization procedure.

Women

We recruited 2560 infertile women (20 to 35 years old) to undergo diagnostic and therapeutic procedures to address their infertility. Of these, 1080 women underwent Lps and Hysc (Group 1), 525 underwent HSG (Group 2), and 955 underwent SH (Group 3).

Analysis

Statistical analysis was carried out with the use of chi-square test. We assessed the specificity and sensitivity of the tests used, their positive and negative predictive values, the likelihood ratio, and the coefficients of agreement (k) (www.statsoft.com).

Results

Women in the three groups (TABLE 2A) did not differ significantly in age (TABLE 2B).

Results of procedures (TABLE 3) are reported here as ongoing pregnancy within 3 years of the start of the diagnostic procedures. Patients studied and treated first with Lps had an overall pregnancy rate of 50% compared with 39% for those who started with HSG and 35% for those who underwent SH as the first diagnostic test (FIG. 1).

TABLE 2B. Mean ages of women whose infertility was investigated with three different diagnostic tests

	Lps	HSG	SH
Means[a]	26.89	27.21	26.57

[a]There were no significant differences between groups analyzed.

Group 1, Lps and Hysc, n = 1080

A. Women with bilateral tubal patency (Group 1A) without another pelvic factor of sterility (n = 580, 54% of the women in Group 1) were subcategorized as follows:

- Group 1A.1 included women who entered the IUI program (n = 390, 67.2% of the women in Group 1A). Eighty-eight women become pregnant in 6 months (22.6%) and a further 85 (21.8%) became pregnant in the subsequent 6 months for a total of 173 pregnancies (44.4%) in 12 months.
- Group 1A.2 included women who entered the IVF–ET program (n = 30, 5.2%). Twenty-two women became pregnant (73.3%), including nine in the first attempt (30%), eight in the second attempt (26.7), and five in the third attempt (16.7%).
- Group 1A.3 included women who waited for a spontaneous pregnancy for 1 more year (n = 150, 25.9%). Twenty-three women become pregnant in 6 months (15.3%) and 47 became pregnant in the 6 subsequent months (31.3%).

If we consider the remaining 99 patients of Group 1A who became pregnant spontaneously between the 12th and 24th months (17.1%), we observe that 342 out

TABLE 3. Pregnancy rates of the subpopulations of women studied according to the initial diagnostic test and the procedure used

Group 1 1080 women underwent Lps	
Group 1A – 580 women (54%) without pelvic factors of sterility	408 women (70%) became pregnant in 6 months to 3 years spontaneously or with ART
Group 1B – 133 women (12%) with bilateral tubal occlusion	58 women (43%) became pregnant within 3 years with surgery and *in vivo* (12%) and/or *in vitro* (42%) procedures
Group 1C – 355 women (33%) with monolateral tubal occlusion	72 women (20%) became pregnant within 3 years with *in vivo* (spontaneous, 27%; IUI, 13%) or *in vitro* (34%) procedures
Group 2 525 women underwent HSG	
Group 2A – 388 women (74%) with bilateral tubal patency	110 women (28%) became pregnant in 6 months to 3 years spontaneously or with *in vivo* (21%) and/or *in vitro* (47%) procedures
Group 2B – 71 women (14%) with bilateral tubal occlusion	49 women (69%) became pregnant within 3 years with *in vitro* procedures
Group 2C – 65 women (12%) with monolateral tubal occlusion	39 women (59%) became pregnant within 3 years with *in vivo* (spontaneous, 7%; IUI, 33%) or *in vitro* (57%) procedures
Group 3 955 women underwent HSG	
Group 3A – 644 women (74%) with bilateral tubal patency	247 women (38%) became pregnant in 6 months to 3 years spontaneously (4%) or with *in vivo* (22%–19%) and/or *in vitro* (54%–51%) procedures
Group 3B – 150 women (16%) with bilateral tubal occlusion	49 women (50%) became pregnant within 3 years with *in vitro* procedures
Group 2C – 144 women (15%) with monolateral tubal occlusion	41 women (28%) became pregnant within 3 years with *in vivo* (IUI, 12%) or *in vitro* (34%) procedures

of 550 women became pregnant spontaneously or with three IUI cycles within 24 months. Out of 238 women who did not become pregnant by *in vivo* methods with or without IUI procedures, 128 underwent IVF–ET as a first or second option for up to three attempts, and 66 of these women (52%) became pregnant in 12 months: 21 in the first attempt (16.4%), 17 in the second attempt (13.3%), and 28 in the third attempt (21.9%). Eighty women of Group 1A (n = 580) had a subfertility factor (a previous history of PID, endometriosis, or adhesions); 45 of these women underwent ART in subgroup 1A, 30 in subgroup 1B, and nine in subgroup 1C. Out of 580 women without male factor or a pelvic factor of sterility, 408 (70%) become pregnant spontaneously or with ART in 6 months to 3 years.

B. One hundred thirty-three women with bilateral tubal occlusion (Group 1B) underwent laparoscopic salpingoplasty; 130 of these women (Group 1B.1) chose the IUI procedure, whereas the other three decided to wait 12 months before entering an IUI program (Group 1B.1). Of the 130 women in Group 1B1, eight women became pregnant with the first attempt, five with the second attempt, and three with the third attempt, for a total of 16 pregnancies in 130 women (12%).

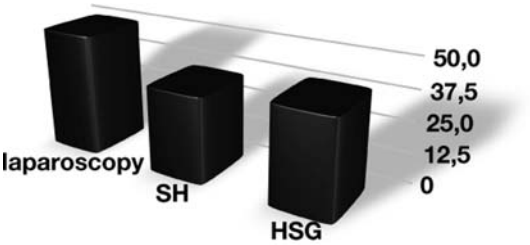

FIGURE 1. Overall pregnancy rates obtained after a diagnosis with Lps, HSG, or SH in the infertile population studied with all types of medical assistance (strategies, procedures, and techniques). The inclusion criteria by Lps are more efficacious than those of HSG and SH.

Of the 114 women who did not become pregnant with the IUI procedure, 102 underwent IVF/ICSI procedures (Group 1B.2) with the following results: 12 become pregnant in the first attempt, 19 in the second attempt, and 11 in the third attempt, for a total of 42 pregnancies in 102 women (42%).

C. Three hundred fifty-five women exhibited mono-

lateral tubal occlusion (Group 1C) with endoscopic signs of PID. Three hundred twenty of these women had a gynecological history supporting the subfertility suspicion.

- Group 1C.1 included 45 women who waited 24 or more months for a spontaneous pregnancy: one of these women became pregnant at 6 months, three at 12 months, and eight at 24 months, for a total of 12 cumulative pregnancies in 45 women (27%).
- Group 1C.2 included 150 women who underwent an IUI program: six of these women became pregnant in the first attempt, nine in the second attempt, and four in the third attempt, for a total of 19 pregnancies in 150 women (13%).
- Group 1C.3 included 160 women who decided to promptly enter an IVF/ICSI program. Only 122 were analyzed, whereas 38 patients dropped out (because of an inadequate ovarian response, psychological issues, a lack of faith in the center's reputation, or relocation to other cities). Out of 122 women, 21 became pregnant in the first cycle, 11 in the second cycle, and nine in the third cycle, for a cumulative total of 41 pregnancies (34%).

D. Twelve women exhibited hysteroscopic features of uterine anatomical abnormalities that did not absolutely preclude spontaneous pregnancy (Group 1D). Three of these women become pregnant spontaneously (including one woman who had a spontaneous abortion at 16 weeks of pregnancy), two became pregnant with IUI, and three with IVF/ICSI (all with live births), for a combined pregnancy rate of 67%.

Endometriosis (stage II–IV of the revised ASRM classification) was diagnosed laparoscopically in 344 out of 1080 women (32%). Only 44 (13%) of the women with endometriosis showed bilateral tubal occlusion.

Group 2, HSG, n = 525

A. Three hundred eighty-eight women presented with bilateral tubal patency (74% of the women in Group 2); of these women, 125 (32.2%) had a past history supporting a risk of subfertility.

- Group 2A.1 included 177 women who underwent IUI. Twelve of these women became pregnant in the first cycle, eight in the second cycle, and five in the third cycle, for a total of 25 pregnancies (14%). Of the 152 women who did not become pregnant, 110 decided to move on to Lps (and Hysc).
- Group 2A.2 included 211 women who decided to wait 3 more months for a spontaneous pregnancy. Eleven pregnancies occurred in the 1st month (5.2%), nine in the 2nd (4.3%), and 10 in the 3rd (4.7%), for a total of 30 pregnancies (14.2%).
  - Out of 181 women who did not become pregnant spontaneously, 122 underwent IUI, and 11 were successful in the first attempt, eight in the second attempt, and nine in the third attempt, for a total of 28 pregnancies (15% cumulative).
  - Fifty-nine women decided to enter directly into an IVF/ICSI program, and 12 became pregnant at the first cycle, seven at the second, and eight at the third, for a total of 27 pregnancies (47%).
  - Out of 126 women who did not become pregnant, 112 underwent Lps.

Laparoscopy and Hysc of 222 women of Group 2A who choose to undergo Lps and Hysc as a second step to address their infertility after HSG (coming from groups 2A.1 and 2A.2) showed the following: bilateral tubal patency in 208 women (94%), monolateral tubal patency in 12 women (5%), bilateral tubal occlusion in two women (1%), PID in 24 women (11%), endometriosis stage II–IV in 68 women (31%), and filmic adhesions around the ovarian–tubal tract without tubal obliteration in 63 women (28%).

B. Seventy-one women with bilateral tubal occlusion (Group 2B; 14% of the women in Group 2) underwent IVF/ICSI programs with 21 pregnancies in the first cycle, 18 in the second cycle, and 10 in the third cycle, for a total of 49 pregnancies (69%). Forty-three of these patients showed a past history supporting a high risk of subfertility.

C. Sixty-six patients with monolateral tubal occlusion (including 49 with left tubal occlusion and 17 with right tubal occlusion) were demonstrated by HSG. Thirty of these patients reported a past history supporting subfertility.

- Group 2C.1 included 60 women seeking a spontaneous pregnancy. One pregnancy occurred after 6 months, two pregnancies after 12 months, and one pregnancy after 24 months.
- Group 2C.2 included six women who underwent IUI. One pregnancy occurred in the first cycle, zero in the second cycle, and one pregnancy occurred in the third cycle.
- Group 2C.3 included the 58 women from Groups 2C.1 and 2C.2 who did not become pregnant and underwent IVF/ICSI. Sixteen pregnancies occurred in the first attempt, 12 in the second, and five in the third, for a total of 33 pregnancies (57%).

Group 3, SH, n = 955

A. We found 644 women with bilateral tubal patency (67%); 123 of these women had a past history supporting subfertility risks.

- Of 341 women (53% of those in Group 3 who had bilateral tubal patency) seeking a spontaneous pregnancy, 19 had become pregnant after the 1st month, 19 after the 2nd month, and 11 after the 3rd month, for a total of 49 pregnancies (4%).
  - Of the 292 women who did not become pregnant spontaneously, 207 underwent IUI. Of these women, 28 had positive results in the first cycle, 18 in the second cycle, and nine in the third cycle, for a total of 55 pregnancies (19%).
  - Eighty-five women decided to directly enter into the IVF/ICSI programs. Twenty-two pregnancies occurred in the first attempt, 11 in the second attempt, and 10 in the third attempt, for a total of 27 pregnancies (51%).
  - Of the 183 women who did not become pregnant spontaneously or with IUI, 116 underwent Lps and Hysc, 43 underwent IVF/ICSI, and 24 dropped out.
- Thirteen women decided to move directly to IVF/ICSI program with four positive results in the first cycle, one in the second cycle, and two in the third cycle, for a total of seven pregnancies (54%).
- Two hundred ninety women were included in the IUI program with the following results: 32 pregnancies in the first cycle, 18 in the second cycle, and 15 in the third cycle, for a total of 65 pregnancies (22%).
  - Of 225 women who did not become pregnant, 132 underwent Lps and Hysc.
  - Of 225 women who did not become pregnant, 93 underwent IVF/ICSI programs with 17 pregnancies after the first attempt, 12 after the second attempt, and 15 after the third attempt, for a total of 44 pregnancies (47%).

Two hundred forty-eight women in Group 3 underwent Lps as a second option. Of these women, 188 (76%) were diagnosed with bilateral tubal patency, 50 (20%) were diagnosed with monolateral tubal patency, 10 (4%) were diagnosed with bilateral tubal occlusion, 33 (13%) were diagnosed with PID, 81 (33%) were diagnosed with endometriosis stage II–IV, and 77 (31%) were diagnosed with filmic adhesions around the ovarian–tubal tract without tubal obliteration.

B. We found 150 women with bilateral tubal occlusion; 123 of these women had a past history supporting subfertility risks.

- Ninety-eight women underwent IVF/ICSI programs with 21 pregnancies after the first cycle, 18 pregnancies after the second cycle, and 10 pregnancies after the third cycle, for a total of 49 pregnancies (50%).
- The other 52 women in Group 3B underwent Lps and Hysc, as did the 49 patients of the previous subgroup who did not become pregnant with the IVF/ICSI program (n = 101). Bilateral tubal occlusion was confirmed in 97 out of 101 women (96%), monolateral tubal patency was found in four of these women (4%), PID was found in 22 women (22%), endometriosis stage II–IV was found in 44 women (44%), and filmic adhesions around the ovarian–tubal tract without tubal obliteration were found in 42 women (42%).

C. We found 154 women with monolateral tubal occlusion; 94 of these women had a past history supporting subfertility risks (these do not total as expected because some women tried more than one approach).

- Sixteen women underwent IUI with one pregnancy in the first cycle, one pregnancy in the second cycle, and zero pregnancies in the third cycle, for a total of two pregnancies (12%).
- One hundred thirty-eight patients underwent Lps with the following results: monolateral tubal occlusion was confirmed in 106 women (%), bilateral tubal patency was found in 21 women (15.2%), and monolateral tubal occlusion (contralateral of that diagnosed in the other women) was found in 11 women (8%).
- After failure of IUI and/or Lps, 137 women decided to move on to IVF/ICSI programs, resulting in 18 pregnancies after the first attempt, 18 after the second attempt, and 11 after the third attempt, for a total of 39 pregnancies (34%).

In addition to the women in Groups 3A–3C above, 17 women underwent SH without diagnosis. Lps and Hysc demonstrated the following: 10 women with bilateral tubal patency, five patients with monolateral tubal patency, two patients with bilateral tubal occlusion, five patients with endometriosis (stage II–IV), and three women with PID, and four women with adhesions.

Sensitivity and Specificity of Tests

Laparoscopy is the gold standard for pelvic factor investigation.

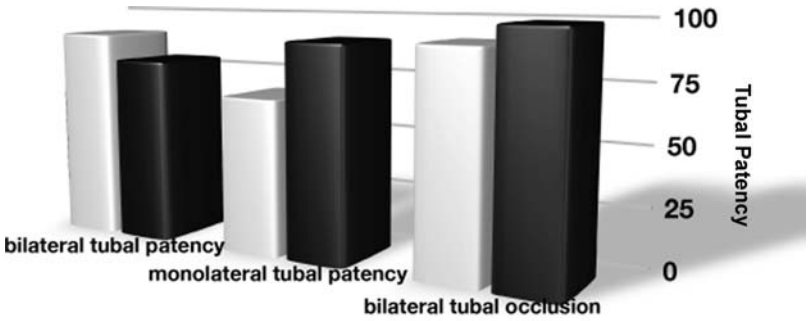

FIGURE 2. Sensitivity and specificity of SH compared with that of Lps (the gold standard). Gray columns indicate the percentage of sensitivity; black columns indicate the percentage of specificity.

Hysterosalpingosonography or Sonohysterosalpingography (SH) (FIG. 2). When bilateral tubal patency was investigated throughout the study, SH sensitivity and specificity—compared with the gold standard—were 89.9% and 78.4%, respectively. The positive and negative predictive values were 75.8% and 91.2%, respectively, and the likelihood ratio was 4.17. The coefficient of agreement (k) was 0.67.

When monolateral tubal patency was investigated with the same technique, the sensitivity and specificity were 66.25% and 90.21%, respectively. The positive and negative predictive values were 76.8% and 90.2%, respectively, and the likewood ratio was 6.77. The coefficient of agreement (K) was 0.58.

When bilateral tubal occlusion was investigated with HSG, the sensitivity and specificity were 90.65% and 98.95%, respectively. The positive and negative predictive values were 95.04% and 97.41%, respectively, and the likewood ratio was 86.12. The coefficient of agreement (K) was 0.91.

Hysterosalpingography (HSG). When bilateral tubal patency was investigated throughout the study, SH sensitivity and specificity—compared with the gold standard—were 86.5% and 79.8%, respectively. The positive and negative predictive values were 71.8% and 88.2%, respectively, and the likelihood ratio was 4.01. The coefficient of agreement (K) was 0.58.

When monolateral tubal patency was investigated with the same technique, the sensitivity and specificity were 64.55% and 88.91%, respectively. The positive and negative predictive values were 71.9% and 80.6%, respectively, and the likelihood ratio was 5.8. The coefficient of agreement (K) was 0.54.

When bilateral tubal occlusion was investigated with HSG, the sensitivity and specificity were 90.05% and 96.91%, respectively. The positive and negative predictive values were 90.02% and 93.61%, respectively, and the likelihood ratio was 80.22. The coefficient of agreement (K) was 0.85.

Discussion

Infertility is commonly defined as a failure to achieve pregnancy during 1 year of frequent, unprotected intercourse. Diagnostic tools are often started after 12 months but can be initiated earlier if infertility is suspected based on a history of endometriosis, previous pelvic surgery, PID, and so forth, or if the female partner is over 35 years old. Major causes of infertility include male factors, ovarian dysfunction, tubal disease, endometriosis, and uterine or cervical factors.[2] Among all the causes of infertility, tubal factors are responsible for almost 15%–30% of female-related infertility[3] and, if we consider pelvic factors to be cumulative of the mechanical obstacles to conception (tubal occlusion and adhesions between ovaries and ampullas), these causes of infertility may be underestimated. The incidence of tubal factor infertility is rapidly increasing with increasing prevalence of salpingitis, sexually transmitted diseases, endometriosis, and so forth.

The assessment of tubal patency is the first mandatory test to employ in the management of infertility. HSG and Lps with chromopertubation are the most common and practical procedures. Sonography–hydrotubation, popularly called hysterosalpingosonography or sonohysterosalpingography (SH) and used to assess tubal patency, provides good visualization of the uterine cavity and myometrial walls in three orthogonal planes. However, some authors suggest that it does not diagnose tubal occlusion or depict the architecture of the fallopian tube as accurately as X-ray HSG[4] or as the gold standard procedure, Lps. The sensitivity and specificity for detecting tubal occlusion was previously reported as 75% and 83%, respectively, with a positive

predictive value of 40% and a negative predictive value of 95%.[4,5]

The aim of the present study was to evaluate the accuracy and efficacy of SH and HSG in the assessment of tubal patency, particularly compared with established methods such as Lps, and to determine their value as basic, noninvasive screening procedures for infertile women. Our results support the intrinsic value of both HSG and SH in diagnosing tubal patency as a first, noninvasive diagnostic test. However, the sensitivity, specificity, and predictive values of both tests do not remove some ethical concerns in the management of infertile patients when the results of these tests are compared with those obtained with Lps. If we consider the goal of these procedures—the live birth—the percentages of women having a baby were higher (FIG. 1) for women who initiated their diagnostic testing with Lps than for those who used indirect diagnostic tests (HSG or SH). Furthermore, the length of time required to have a baby was prolonged in patients who did not choose Lps as their first diagnostic test. This difference might occur because Lps is often both diagnostic and operative and it may provide for the solution itself. A delay in reaching a diagnosis regarding the cause of infertility is most problematic when we choose indirect diagnostic tests instead of Lps. In fact, the most critical parameter for the efficacy of a cure for infertility is the age of the woman. Any delay in initiating a therapeutic approach may risk a reduction in its efficacy. However, when we are choosing the most appropriate test to establish possible causes of infertility, we should also consider that Lps is a risky procedure. The mortality rate is 3.33 per hundred thousand laparoscopies. The overall complication rate is 4.64 per thousand laparoscopies, and the rate of complications requiring laparotomy is 3.20 per thousand.[1] It is clear from the present study that, following indirect tests (HSG and SH), significant percentages of patients with positive tubal tests did not conceive based on false positive tubal tests and/or a lack of diagnosis of several pelvic factors (e.g., ovarian filmic adhesions; FIG. 3) that are recognized by the use of direct tubal patency tests.

Despite high values of sensitivity and specificity of HSG and SH, as well as their positive and negative predictive values, we should point out the meaning of these statistical evaluations: they report values of the correspondence of tubal patency/tubal occlusion results between either HSG or SH and Lps. But for a successful pregnancy, oocytes must leave the ovaries and enter the ampullas before entering the tubal lumen. Indirect tests do not provide information regarding pelvic factors of infertility other than tubal patency (FIG. 3). The infertile women in our population are often over 35 years old. Is it reasonable to encourage these women to use indirect tests to establish the presence of a pelvic factor of infertility if we consider that the ART procedures and their success rates (*in vivo* or IVF) depend on a complete diagnosis of the pelvic factors of sterility rather than only on the presence of a tubal patency? Can we offer the couple a noninvasive test to establish a consequent therapeutic procedure that may fail just because we failed in recognizing the pelvic condition? Infections, endometriosis, and previous pelvic surgery are common histories of patients with infertility, and an incorrect diagnosis may result in a dramatic delay in the use of the appropriate therapeutic procedure (e.g., IVF–ET in older women). Endometriosis is one of the possible causes of pelvic factor infertility; it reduces fecundity in normal couples from 0.15–0.20 a unit per month[6,7] to 0.02–0.1 a unit per month.[8]

We know that infertile women have 6 to 8 times the rate of endometriosis compared with fertile women.[9] Why? We do not have clear answer, but pelvic factors represent a possibility. From 25% to 50% of infertile women have endometriosis and from 30% to 50% of women with endometriosis are infertile.[10] There is a strong prevalence of endometriosis in infertile women compared with fertile women undergoing tubal sterilization (5%),[11] and similar findings have been reported with pelvic infections. In our study, endometriosis (stage II–IV of the revised ASRM classification) was diagnosed laparoscopically in 344 out of 1080 women (32%), and only 44 women with endometriosis showed bilateral tubal occlusion (13%). Only Lps, not HSG or SH, is effective in diagnosing endometriosis. The surgical removal of endometriotic implants improves the fertility of women, as indicated by two randomized controlled studies.[12,13] Often, the removal is associated with adhesiolysis. Lps is useful in diagnosing the disease and in removing the implants of endometriosis, shortening the length of time required to cure the infertility.

Although various mechanisms have been proposed as causes of endometriosis-associated sterility, pelvic anatomy distortion is the most convincing one. The so-called pelvic factor of sterility associated with endometriosis is a common observation in laparoscopic practice. However, functional disorders of the eutopic endometrium may be closely associated with the presence of ectopic endometrium (e.g., abnormal uterine contraction resulting from the cascade of biochemical products released after irritation and inflammation in pelvic structures, such as prostaglandins). A diagnosis of pelvic signs of endometriosis, PID, and previous surgery may indicate the need for further therapeutic procedures before or after ART and during ART

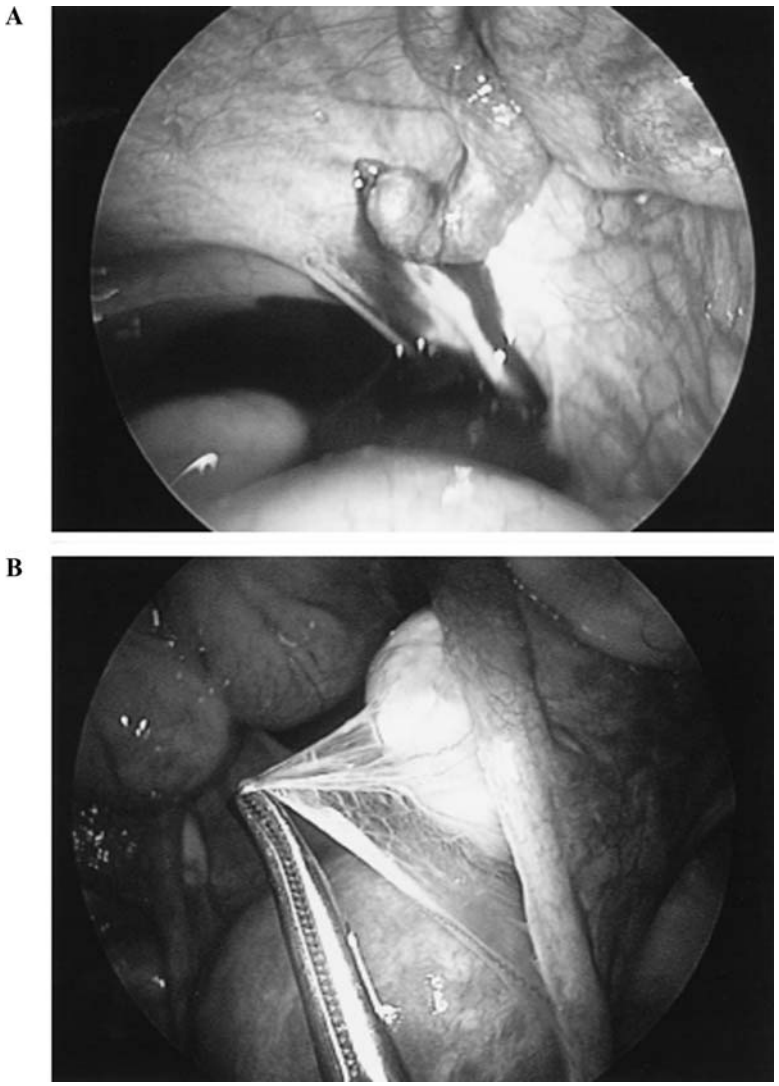

FIGURE 3. Tubal patency does not always support women's fertility. Tubal ampullas **(A)** may not be anatomically able to allow for oocytes' descent into the tubal lumen, and the ovary **(B)** may be coated from filmic adhesions that stop the oocytes' descent throughout the tubes themselves. These are common pelvic features that can be obstacles to having a baby but that HSG and SH do not diagnose. Is it ethically acceptable to use HSG or SH in a patient over 35 years old with the recognized risk of delaying her pregnancy and resulting in a lost opportunity?

procedures. Structural or inflammatory damage to the pelvic environment are thought to preclude the use of *in vivo* attempts to conceive, for their intrinsic delay greatly reduces the chance of a successful pregnancy. An adverse immunochemical environment is another theory proposed to explain the decreased fertility of these women,[14] and evidence of this altered environment is very often detectable by a simple pelvic examination. The diagnosis of endometriosis is based on The Revised Classification of AFS,[15] at least when the main goal is to score it for a fertility prognosis.

When the infertile couple is considering counseling, female age, duration of infertility, male factor, history of pelvic pain, the stage of diagnosed endometriosis, and family history should be taken into account in planning the clinical management of infertility, with specific attention to the prognosis and the time required to implement the chosen therapeutic strategy.

All patients over 30 years old with a history of pelvic infections, endometriosis, and/or previous pelvic surgery should be advised to undergo Lps instead of indirect tubal tests. Superovulation and IUI should be used to achieve pregnancy, as well as IVF, according to age, sperm count, laparoscopic findings of the pelvic reproductive organs, and ovarian responsivity.[14] The higher risks of Lps[1] as a diagnostic tool for infertility, compared with HSG and SH, should also be described to patients, as should its added value in conjunction with therapeutic approaches to infertility.

Conflicts of Interest

The authors declare no conflicts of interest.

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